

Claims:

1. An isolated nucleic acid molecule encoding a mammalian TIE ligand,
(a) selected from the group consisting of human NL-1 (SEQ. ID. NO: 2), human NL-5 (SEQ. ID. NO: 4), human NL8 (SEQ. ID. NO: 6), and homologs thereof in a non-human mammalian species; or
(b) a biologically active functional derivative thereof,
provided that if the functional derivative is an amino acid sequence variant, it has at least about 90% sequence identify with the fibrinogen-like domain of a human NL-1, human NL-5 or human NL8 ligand.
2. The isolated nucleic acid molecule of claim 1 which comprises the coding region of SEQ. ID. NO: 1; SEQ. ID. NO: 3; or SEQ. ID. NO: 5.
3. The isolated nucleic acid molecule of claim 1 which comprises the fibrinogen-like domain of SEQ. ID. NO: 1; SEQ. ID. NO: 3; or SEQ. ID. NO: 5.
4. A vector which comprises a nucleic acid molecule of claim 1.
5. A recombinant host cell transformed with a nucleic acid molecule according to claim 1.
6. The recombinant host cell of claim 5 which is a prokaryotic cell.
7. The recombinant host cell of claim 5 which is a eukaryotic cell.
8. An isolated mammalian TIE ligand,

(a) selected from the group consisting of human NL-1 (SEQ. ID. NO: 2), human NL-5 (SEQ. ID NO: 4), human NL8 (SEQ. ID. NO: 6), and homologs thereof in a non-human mammalian species; or

(b) a biologically active functional derivative thereof,
 5 provided that if the functional derivative is an amino acid sequence variant, it has at least about 90% sequence identity with the fibrinogen-like region of a human NL-1, human NL-5 or human NL-8 ligand.

10 *a* 9. An antibody which specifically binds the ^{*polypeptide*}~~TIE ligand~~ according to claim 8.

10. The antibody of claim 9 which is a monoclonal antibody.

11. The antibody of claim 10 which is an antagonist of the TIE-2 receptor.

15 12. The antibody of claim 10 which is an agonist of the TIE-2 receptor.

13. A composition comprising a ^{*polypeptide*}~~TIE ligand~~ according to claim 8 or an antibody according to claim 9, in association with a carrier.

20 *a* 14. A conjugate comprising a ^{*polypeptide*}~~TIE ligand~~ according to claim 8 or an antibody according to claim 9, fused to a further therapeutic or cytotoxic agent.

25 15. The conjugate of claim 14 wherein the further therapeutic agent is a toxin, another TIE ligand, or a member of the vascular endothelial growth factor (VEGF) family.

16. A method for identifying a cell expressing a TIE receptor comprising contacting the cell with a detectably labeled TIE ligand according to claim 8 under conditions permitting the binding of said TIE ligand to the TIE receptor, and monitoring the binding.

17. A method for identifying an antagonist of a TIE receptor, comprising contacting cells expressing the TIE receptor with a TIE ligand according to claim 8 and a test compound, under conditions permitting the binding of said TIE ligand to the TIE receptor, and determining whether the test compound is capable of interfering with the binding of the TIE ligand to the TIE receptor.

18. A method for imaging the presence of angiogenesis, which comprises administering to a patient a detectably labeled TIE ligand according to claim 8, or antibody agonist according to claim 9 of a TIE receptor, and monitoring angiogenesis.

19. A method for inhibiting vasculogenesis, comprising administering to a patient an effective amount of a TIE ligand according to claim 8.

20. The method of claim 19 wherein said TIE ligand is a native human NL8 molecule.

21. A method of inhibiting tumor growth, comprising administering to a patient an effective amount of a TIE ligand according to claim 8.

22. A method for promoting bone development, maturation or growth, comprising administering to a patient in need an effective amount of TIE ligand according to claim 8.

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